

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Bruce A. Yankner and Philip Nadeau

Serial No.: Divisional of 09/239,387

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No. EL 778 571 835 US

Filed: February 28, 2002

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For: METHODS FOR DECREASING BETA AMYLOID PROTEIN

Box Patent Application
Commissioner of Patents and Trademarks
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Prior to examination, please amend the application as follows.

In the Specification

On page 1, after the title and before the heading "Background of the
Invention", please insert the following heading and paragraph.

--Cross-Reference to Related Applications

This application is a divisional of pending prior application U.S. Serial
No. 09/239,387 filed January 28, 1999, which is a divisional of U.S. Serial
No. 09/046,235 filed March 23, 1998, now U.S. Patent No. 6,080,778. The United
States government has certain rights in this invention by virtue of National
Institutes of Health grant number RO1NS33325 to Bruce A. Yankner.--

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On page 1, lines 3-5, please delete the sentence beginning with "The United States government", and ending with "Bruce A. Yankner."

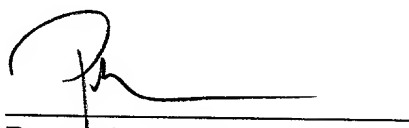
In the Claims

Please delete claims 1-22.

Remarks

Applicants have enclosed a copy of the claims as pending upon entry of the Preliminary Amendment. Applicants have also enclosed a marked-up version of amended specification page 1 pursuant to 37 C.F.R. § 1.121(b)(1)(iii), and a clean copy of amended specification page 1 pursuant to 37 C.F.R. § 1.121(b)(1)(ii).

Respectfully submitted,



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Claims As Pending Upon Entry of Preliminary Amendment

23. A composition for decreasing the production of A β comprising an effective amount of a compound to decrease blood cholesterol levels.
24. The composition of claim 23 comprising an HMG CoA reductase inhibitor.
25. The composition of claim 24 wherein the inhibitor is selected from the group consisting of lovastatin, simvastatin, fluvastatin, pravastatin, atorvastatin, cerivastatin, and compactin.
26. The composition of claim 23 comprising a compound which inhibits uptake of dietary cholesterol.
27. The composition of claim 23 wherein the composition blocks or decreases endogenous cholesterol production.
28. The composition of claim 27 wherein the composition comprises an inhibitor of the cholesterol biosynthetic enzymes selected from the group consisting of 2,3-oxidosqualene cyclase, squalene synthase, and 7-dehydrocholesterol reductase.
29. The composition of claim 23 wherein the composition is selected from the group consisting of a fibrate, a bile acid binding resin, probucol, nicotinic acid, garlic or garlic derivative, and psyllium.

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CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.10

I hereby certify that this paper and any documents referred to as attached or enclosed are being deposited with the United States Postal Service on this date, February 28, 2002, in an envelope as "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10, Express Mail Label No. EL 778 571 835 US, addressed to Box Patent Application, Commissioner of Patents and Trademarks, Washington, D.C. 20231.



Pam Turnbough

Date: February 28, 2002

ATL1 #504917 v1

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METHODS FOR DECREASING BETA AMYLOID PROTEIN

Cross-Reference to Related Applications

This application is a divisional of pending prior application U.S. Serial No. 09/239,387 filed January 28, 1999, which is a divisional of U.S. Serial No. 09/046,235 filed March 23, 1998, now U.S. Patent No. 6,080,778. The United States government has certain rights in this invention by virtue of National Institutes of Health grant number RO1NS33325 to Bruce A. Yankner.

Background of the Invention

[The United States government has certain rights in this invention by virtue of National Institutes of Health grant number RO1NS33325 to Bruce A. Yankner.]

Alzheimer's disease (AD) is the most common cause of dementia in the aged population. The accumulation of large numbers of senile plaques containing the 40-42 amino acid amyloid β protein ($A\beta$) is a classic pathological feature of AD. Both genetic and cell biological findings suggest that the accumulation of $A\beta$ in the brain is the likely cause of AD (Yankner, B.A. (1996) Neuron 16, 921-932.; Selkoe, D.J. Science 275, 630-631 (1997)). Strong genetic evidence in support of the pathogenic role of $A\beta$ came from the observation that individuals who inherit mutations in the amyloid precursor protein almost invariably develop AD at an early age. These mutations increase the production of a long variant of the $A\beta$ peptide that forms senile plaques in the brain (Goate et al., (1991) Nature 349, 704-706). Mutations and allelic variations in other genes that cause AD, including the presenilins and apolipoprotein E, also result in increased production or deposition of the $A\beta$ peptide. Reiman, et al. (1996) N.E.J.Med. 334, 752-758, reported that in middle age, early to mid 50's, individuals who are homozygous for the Apo E4 gene have reduced glucose metabolism in the same regions of the brain as in patients with Alzheimer's disease. These findings suggest that the pathological changes

Clean Copy of Amended Specification Page 1
Pursuant to 37 C.F.R. § 1.121(b)(1)(ii)

1. The present invention relates to a method of determining the concentration of a substance in a sample. The method involves measuring the absorbance of the sample at a specific wavelength and comparing it to a standard curve. The standard curve is generated by measuring the absorbance of known concentrations of the substance. The concentration of the substance in the sample is then determined by finding the point on the standard curve that corresponds to the measured absorbance.

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 25 with Alzheimer's disease. These findings suggest that the pathological changes in the brain associated with this gene start early. Furthermore, individuals with Down's syndrome overexpress the amyloid precursor protein, develop $A\beta$ deposits in the brain at an early age, and develop Alzheimer's disease at an early age. Finally, the $A\beta$ protein has been demonstrated to be highly toxic to nerve